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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: T1R TASTE RECEPTORS AND GENES ENCODING SAME

(57) Abstract: Newly identified mammalian taste-cell-specific G protein-coupled receptors, and the genes and cDNA encoding said receptors are described. Specifically, T1R G protein-coupled receptors active in taste signaling, and the genes and cDNA encoding the same, are described, along with methods for isolating such genes and for isolating and expressing such receptors. Methods for representing taste perception of a particular taste stimulus in a mammal are also described, as are methods for generating novel molecules or combinations of molecules that elicit a predetermined taste perception in a mammal, and methods for simulating one or more tastes. Further, methods for stimulating or blocking taste perception in a mammal are also disclosed.

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INTERNATIONAL SEARCH REPORT

onal Application No
PCT/US 02/00198

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/705 C12N15/12 C12N15/62 C07K16/18 C12Q1/68
C12N5/10 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, EMBL, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOON M A ET AL: "PUTATIVE MAMMALIAN TASTE RECEPTORS: A CLASS OF TASTE-SPECIFIC GPCRS WITH DISTINCT TOPOGRAPHIC SELECTIVITY" CELL, MIT PRESS, CAMBRIDGE, MA,, US, vol. 96, 19 February 1999 (1999-02-19), pages 541-551, XP000922524 ISSN: 0092-8674 the whole document --- -/--	1-3, 7-13, 17-23, 27-33, 37-43, 47-55, 59-67, 71-79, 83-91, 95-104, 108-178, 182-188, 192-199, 204-212, 216-234

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 November 2003	09/12/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mueller, F

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INTERNATIONAL SEARCH REPORT

Int onal Application No
PCT/US 02/00198

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	LI XIAODONG ET AL: "Human receptors for sweet and umami taste" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 99, no. 7, 2 April 2002 (2002-04-02), pages 4692-4696, XP002254830 ISSN: 0027-8424 the whole document ---	1-3, 7-13, 17-23, 27-33, 37-43, 47-55, 59-67, 71-79, 83-91, 95-104, 108-178, 182-188, 192-199, 204-212, 216-234
X	WO 95 08627 A (CIBA GEIGY AG ;FLOR PETER JOSEF (DE); KUHN RAINER (DE); LINDAUER K) 30 March 1995 (1995-03-30) the whole document ---	1-3, 7-13, 17-23, 27-33, 37-43, 47-55, 59-67, 71-79, 83-91, 95-104, 108-178, 182-188, 192-199, 204-212, 216-234
X	DATABASE EMBL 'Online! embl heidelberg; Acc#: AC062024, 21 June 2000 (2000-06-21) XP002262036 99,721% identity in 1739 bp overlap to claimed seq id 15. the whole document ---	1-3, 7-13, 17-23, 27-33, 37-43, 47-55, 59-67, 71-79, 83-91, 95-104, 108-178, 182-188, 192-199, 204-212, 216-234

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 02/00198

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	ADLER E ET AL: "A NOVEL FAMILY OF MAMMALIAN TASTE RECEPTORS" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 100, no. 6, 17 March 2000 (2000-03-17), pages 693-702, XP000982304 ISSN: 0092-8674 cited in the application the whole document	1-3, 7-13, 17-23, 27-33, 37-43, 47-55, 59-67, 71-79, 83-91, 95-104, 108-178, 182-188, 192-199, 204-212, 216-234

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NSDOCID: <WO 02064631A3 I >

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 02/00198

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.:
4,5,6,14,15,16,24,25,26,34,35,36,44,45,46,56,57,58,68,69,70,80,81,82,92,93,94,105,106,107,179,180etc

Present claims
4,5,6,14,15,16,24,25,26,34,35,36,44,45,46,56,57,58,68,69,70,80,81,82,92,93,94,105,106,107,179,180,181,189,190,191,201,202,203,213,214,215,relate to an extremely large number of possible compounds/products/apparatus/methods. In fact, the claims contain so many options, variables, possible permutations and provisos that a lack of clarity (and/or conciseness) and support within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, no search has been carried out for those parts of the application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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TCGGCCCCAAGTGCTACATGATCCTCTTCTACCCGGAGCGCAACACGCCCG CCTACTTCAACAGCATGATCCAGGGCTACACCATGAGGAGGGACTAG (SEQ ID NO. 20)

hT1R2 conceptual translation (SEQ ID NO 21)

MGPRAKTICSLFFLLWVLAEPAENSDFYLPGDYLLGGLFSLHANMKGIVHLNFLQ VPMCKEYEVKVIGYNLMQAMRFAVEEINNDSSLLPGVLLGYEIVDVCYISNNVQP VLYFLAHEDNLLPIQEDYSNYISRVVAVIGPDNSESVMTVANFLSLFLLPQITYSAI SDELRDKVRFPALLRTTPSADHHVEAMVQLMLHFRWNWIIVLVSSDTYGRDNGQ LLGERVARRDICIAFQETLPTLQPNQNMTSEERQRLVTIVDKLQQSTARVVVVFS PDLTLYHFFNEVLRQNFTGAVWIASESWAIDPVLHNLTELGHLGTFLGITIQSVPIP GFSEFREWGPQAGPPPLSRTSQSYTCNQECDNCLNATLSFNTILRLSGERVVYS VYSAVYAVAHALHSLLGCDKSTCTKRVVYPWQLLEEIWKVNFTLLDHQIFFDPQG DVALHLEIVQWQWDRSQNPFQSVASYYPLQRQLKNIQDISWHTVNNTIPMSMC SKRCQSGQKKKPVGIHVCCFECIDCLPGTFLNHTEDEYECQACPNNEWSYQSE TSCFKRQLVFLEWHEAPTIAVALLAALGFLSTLAILVIFWRHFQTPIVRSAGGPMC FLMLTLLLVAYMVVPVYVGPPKVSTCLCRQALFPLCFTICISCIAVRSFQIVCAFKM ASRFPRAYSYWVRYQGPYVSMAFITVLKMVIVVIGMLATGLSPTTRTDPDDPKITI VSCNPNYRNSLLFNTSLDLLLSVVGFSFAYMGKELPTNYNEAKFITLSMTFYFTSS VSLCTFMSAYSGVLVTIVDLLVTVLNLLAISLGYFGPKCYMILFYPERNTPAYFNS MIQGYTMRRD (SEQ ID NO. 21)

Example 7

Methods for Heterologous Expression of T1Rs in Heterologous Cells

[0226] An HEK-293 derivative (Chandrashekar et al., Cell 100(6): 703-11 (2000)), which stably expresses Gα15, was grown and maintained at 37°C in Dulbecco's Modified Eagle Medium (DMEM, Gibco BRL) supplemented with 10% FBS, MEM non-essential amino acids (Gibco BRL), and 3 μg/ml blasticidin. For calcium-imaging experiments, cells were first seeded onto 24-well tissue-culture plates (approximately 0.1 million cells per well), and transfected by lipofection with Mirus TransIt-293 (PanVera). To minimize glutamate-induced and glucose-induced desensitization, supplemented DMEM was replaced with low-glucose DMEM/GlutaMAX (Gibco BRL) approximately 24 hours after transfection. 24 hours later, cells were loaded with the calcium dye Fluo-4 (Molecular Probes), 3μM in Dulbecco's PBS buffer (DPBS, GibcoBRL), for 1.5 hours at room temperature.

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After replacement with 250µl DPBS, stimulation was performed at room temperature by addition of 200µl DPBS supplemented with taste stimuli. Calcium mobilization was monitored on a Axiovert S100 TV microscope (Zeiss) using Imaging Workbench 4.0 software (Axon). T1R1/T1R3 and T1R2/T1R3 responses were strikingly transient – calcium increases rarely persisted longer than 15 seconds – and asynchronous. The number of responding cells was thus relatively constant over time; therefore, cell responses were quantitated by manually counting the number of responding cells at a fixed time point, typically 30 seconds after stimulus addition.

Example 8

Human T1R2/T1R3 functions as a sweet taste receptor

[0227] HEK cells stably expressing Gα15 were transiently transfected with human T1R2, T1R3 and T1R2/T1R3, and assayed for increases in intracellular calcium in response to increasing concentrations of sucrose (Figure 1(a)). Also, T1R2/T1R3 dose responses were determined for several sweet taste stimuli (Figure 1(b)). The maximal percentage of responding cells was different for different sweeteners, ranging from 10-30%. For clarity, dose responses were normalized to the maximal percentage of responding cells. The values in Figure 1 represent the mean ± s.e. of four independent responses. X-axis circles mark psychophysical detection thresholds determined by taste testing. Gurmarin (50-full dilution of a filtered 10g/l *Gymnema sylvestre* aqueous extract) inhibited the response of T1R2/T1R3 to 250 mM sucrose, but not the response of endogenous β2-adrenergic receptor to 20 μM isoproterenol (Figure 1(b)). Figure 1(c) contains the normalized response of T1R2/T1R3 co-expressing cell lines to different sweeteners(sucrose, aspartame, tryptophan and saccharin)

EXAMPLE 9

Rat T1R2/T1R3 also functions as a sweet taste receptor

[0228] HEK cells stably expressing Gα15 were transiently transfected with hT1R2/hT1R3, rT1R2/rT1R3, hT1R2/rT1R3, and rT1R2/hT1R3. These transfected cells were then assayed for increased intracellular calcium in response to 350 mM sucrose, 25 mM tryptophan, 15 mM aspartame, and 0.05 of monellin. The results with sucrose and aspartame are contained in Figure 2 and indicate

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that rT1R2/rT1R3 also functions as a sweet taste receptor. Also, these results suggest that T1R2 may control T1R2/T1R3 ligand specificity.

EXAMPLE 10

Human T1R1/T1R3 functions as umami taste receptors

[0229] HEK cells stably expressing Gα15 were transiently transfected with human T1R1, T1R3 and T1R1/T1R3 and assayed for increases in intracellular calcium in response to increasing concentrations of glutamate (Figure 3(a) and 0.5 mM glutamate), 0.2 mM IMP, and 0.5 mM glutamate plus 0.2 mM IMP (Figure 3(b)). Human T1R1/T1R3 dose responses were determined for glutamate in the presence and absence of 0.2 mM IMP (Figure 3(c)). The maximal percentages of responding cells was approximately 5% for glutamate and approximately 10% for glutamate plus IMP. For clarity, does responses are normalized to the maximal percentage of responding cells. The values represent the mean $\pm$ s.e. of four independent responses. X-axis circles mark taste detection thresholds determined by taste testing.

EXAMPLE 11

PDZIP as an Export Sequence

[0230] The six residue PDZIP sequence (SVSTW (SEQ ID NO:22)) was fused to the C-terminus of hT1R2 and the chimeric receptor (i.e. hT1R2-PDZIP) was transfected into an HEK-293 host cell. The surface expression of hT1R2 was then monitored using immunofluorescence and FACS scanning data. As shown in Figures 6A and 6B, the inclusion of the PDZIP sequence increased the surface expression of hT1R2-PDZIP relative to hT1R2.

PKZIP Sequence

SVSTVV (SEQ ID NO:22)

[0231] More specifically, Figure 4A shows an immunofluorescence staining of myc-tagged hT1R2 demonstrating that PDZIP significantly increases the amount of hT1R2 protein on the plasma membrane. Figure 4B shows FACS analysis data demonstrating the same result.– Cells expressing myc-tagged hT1R2 are indicated by the dotted line and cells expressing myc-tagged hT1R2-PDZIP are indicated by the solid line.

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Example 12

Generation of Cell Lines that Stably Co-Express T1R1/T1R3 or T1R2/T1R3

[0232] Human cell lines that stably co-express human T1R2/T1R3 or human T1R1/T1R3 were generated by transfecting linearized PEAK10-derived (Edge Biosystems) vectors containing pCDNA 3.1/ZEO-derived (Invitrogen) vectors respectively containing hT1R1 or hT1R2 expression construct (plasmid SAV2485 for T1R1, SAV2486 for T1R2) and hT1R3 (plasmid SXV550 for T1R3) into a $G_{\alpha 15}$ expressing cell line. Specifically, T1R2/T1R3 stable cell lines were produced by co-transfecting linearized SAV2486 and SXV550 into Aurora Bioscience's HEK-293 cell line that stably expresses $G_{\alpha 15}$. T1R1/T1R3 stable cell lines were produced by co-transfecting linearized SAV2485 and SXV550 into the same HEK-293 cell line that stably expresses $G_{\alpha 15}$. Following SAV2485/SCV550 and SAV2486/SXV550 transfections, puromycin-resistant and zeocin-resistant colonies were selected, expanded, and tested by calcium imaging for responses to sweet or umami taste stimuli. Cells were selected in 0.0005 mg/ml puromycin (CALBIOCHEM) and 0.1 mg/ml zeocin (Invitrogen) at 37°C in low-glucose DMEM supplemented with GlutaMAX, 10% dialyzed FBS, and 0.003 mg/ml blasticidin. Resistant colonies were expanded, and their responses to sweet taste stimuli evaluated by Fluorescence microscopy. For automated fluorimetric imaging on VIPR-II instrumentation (Aurora Biosciences), T1R2/T1R3 stable cells were first seeded onto 96-well plates (approximately 15,000 cells per well). Twenty-four hours later, cells were loaded with the calcium dye fluo-3-AM (Molecular Probes), 0.005 mM in PBS, for one hour at room temperature. After replacement with 70 ml PBS, stimulation was performed at room temperature by addition of 70 ml PBS supplemented with taste stimuli. Fluorescence (480 nm excitation and 535 nm emission) responses from 20 to 30 seconds following compound addition were averaged, corrected for background fluorescence measured prior to compound addition, and normalized to the response to 0.001 mM ionomycin (CALBIOCHEM), a calcium ionophore.

[0233] It was then observed that when these cell lines were contacted with sweet or umami, that for active clones typically 80-100% of cells responded to taste stimuli. Unexpectedly, the magnitude of individual cell responses was markedly larger than that of transiently transfected cells.

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[0234] Based on this observation, the inventors tested the activity of T1R stable cell lines by automated fluorescence imaging using Aurora Bioscience's VIPR instrumentation as described above. The responses of two T1R1/T1R3 and one T1R2/T1R3 cell line are shown in Figure 5 and Figure 6 respectively.

[0235] Remarkably, the combination of increased numbers of responding cells and increased response magnitudes resulted in a greater than 10-fold increase in activity relative to transiently transfected cells. (By way of comparison, the percent ionomycin response for cells transiently transfected with T1R2/T1R3 was approximately 5% under optimal conditions.) Moreover, dose responses obtained for stably expressed human T1R2/T1R3 and T1R1/T1R3 correlated with human taste detection thresholds. The robust T1R activity of these stable cell lines suggests that they are well suited for use in high-throughput screening of chemical libraries in order to identify compounds, e.g. small molecules, that modulate the sweet or umami taste receptor and which therefore modulate, enhance, block or mimic sweet or umami taste.

[0236] While the foregoing detailed description has described several embodiments of the present invention, it is to be understood that the above description is illustrative only and not limiting of the disclosed invention. The invention is to be limited only by the claims which follow.

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WHAT IS CLAIMED:

1. An isolated nucleic acid selected from the group consisting of:

(i) a genomic DNA sequence consisting essentially of a nucleic acid sequence coding for a T1R mammalian G protein-coupled receptor polypeptide active in taste signaling, wherein said nucleic acid sequence consists essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20;

(ii) a genomic DNA sequence consisting essentially of a nucleic acid sequence coding for a T1R mammalian G protein-coupled receptor polypeptide have an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21;

(iii) a genomic DNA sequence having at least about 50% identity to a nucleic acid sequence coding for a T1R mammalian G protein-coupled receptor polypeptide, wherein said nucleic acid sequence consists essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20; a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20

(iv) a genomic DNA sequence consisting essentially of a nucleic acid sequence coding for a T1R mammalian G protein-coupled receptor polypeptide having an amino acid sequence that is at least about 40% identical to the amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21;

(v) a genomic DNA sequence consisting essentially of a sequence coding for a T1R mammalian G protein-coupled receptor polypeptide comprising a consensus sequence selected from the group consisting of SEQ ID NOs 18 and 19, and sequences having at least about 75% identity to SEQ ID NOs 18 or 19;

(vi) a cDNA sequence having the same nucleic acid sequence as the T1R mammalian G protein-coupled receptor polypeptide coding region in the genomic DNA sequence selected from the group consisting of SEQ ID NOs 15 and 20;

(vii) a cDNA sequence coding for a T1R mammalian G protein-coupled receptor polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21;

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(viii) a cDNA sequence coding for a T1R mammalian G protein-coupled receptor polypeptide comprising a consensus sequence selected from the group consisting of SEQ ID NOs 18 and 19, and sequences having at least about 75% identity to SEQ ID NOs 18 or 19;

(ix) a cDNA sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20;

(x) a cDNA sequence having at least about 50% sequence identity to the T1R G protein-coupled receptor polypeptide coding region in the genomic DNA sequence selected from the group consisting of SEQ ID NOs 15 and 20;

(xi) a cDNA sequence having at least about 50% sequence identity to a sequence encoding a T1R mammalian G protein-coupled receptor polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21;

(xii) a cDNA sequence having at least about 50% identity to a sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20;

(xiii) a variant of a nucleotide sequence selected from the group consisting of SEQ ID NOs 3, 13, 15, 16, and 20, containing at least one conservative substitution in a region coding for a T1R G protein-coupled receptor polypeptide active in taste signaling;

(xiv) a variant of a nucleotide sequence encoding a T1R G protein-coupled receptor polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21, containing at least one conservative substitution in a T1R mammalian G protein-coupled receptor polypeptide coding region; and

(xv) a variant of a cDNA sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20, containing at least one conservative substitution.

2. An isolated genomic DNA molecule consisting essentially of a nucleic acid sequence coding for a mammalian G protein-coupled receptor polypeptide, wherein said nucleic acid sequence consists essential of SEQ ID NO 15 or 20.

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3. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 2.

4. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 2 under stringent hybridization conditions.

5. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 2 under moderate hybridization conditions.

6. An isolated fragment of the genomic DNA molecule of claim 2 that is at least about 20 to 30 nucleotide bases in length.

7. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 2, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

8. The chimeric or fused nucleic acid molecule of claim 7, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

9. The chimeric or fused nucleic acid molecule of claim 7, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

10. The chimeric or fused nucleic acid molecule of claim 9, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

11. The chimeric or fused nucleic acid molecule of claim 7, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

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12. An isolated genomic DNA molecule consisting essentially of a nucleic acid sequence coding for a mammalian G protein-coupled receptor having an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21.

13. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 12.

14. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 12 under stringent hybridization conditions.

15. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 12 under moderate hybridization conditions.

16. An isolated fragment of the genomic DNA molecule of claim 12 that is at least about 20 to 30 nucleotide bases in length.

17. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 12, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

18. The chimeric or fused nucleic acid molecule of claim 17, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

19. The chimeric or fused nucleic acid molecule of claim 17, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

20. The chimeric or fused nucleic acid molecule of claim 19, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

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21. The chimeric or fused nucleic acid molecule of claim 17, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

22. An isolated genomic DNA molecule consisting essentially of a nucleic acid sequence having at least about 50% identity to a nucleic acid sequence coding for a mammalian G protein-coupled receptor polypeptide, wherein said nucleic acid sequence consists essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20.

23. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 22.

24. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 22 under stringent hybridization conditions.

25. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 22 under moderate hybridization conditions.

26. An isolated fragment of the genomic DNA molecule of claim 22 that is at least about 20 to 30 nucleotide bases in length.

27. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 22, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

28. The chimeric or fused nucleic acid molecule of claim 27, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

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29. The chimeric or fused nucleic acid molecule of claim 27, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

30. The chimeric or fused nucleic acid molecule of claim 29, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

31. The chimeric or fused nucleic acid molecule of claim 27, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

32. An isolated genomic DNA molecule consisting essentially of a nucleic acid sequence coding for a mammalian G protein-coupled receptor having an amino acid sequence that is at least about 40% identical to the amino acid sequence selected from the group consisting of SEQ ID NO: 4, 14, 17, and 21.

33. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 32.

34. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 32 under stringent hybridization conditions.

35. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 32 under moderate hybridization conditions.

36. An isolated fragment of the genomic DNA molecule of claim 32 that is at least about 20 to 30 nucleotide bases in length.

37. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 32, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

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38. The chimeric or fused nucleic acid molecule of claim 37, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

39. The chimeric or fused nucleic acid molecule of claim 37, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

40. The chimeric or fused nucleic acid molecule of claim 39, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

41. The chimeric or fused nucleic acid molecule of claim 37, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

42. An isolated cDNA molecule comprising a nucleic acid sequence having the same sequence as the mammalian G protein-coupled receptor polypeptide coding region contained in a genomic DNA sequence consisting essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20.

43. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 42.

44. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 42 under stringent hybridization conditions.

45. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 42 under moderate hybridization conditions.

46. An isolated fragment of the genomic DNA molecule of claim 42 that is at least about 20 to 30 nucleotide bases in length.

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47. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 42, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

48. The chimeric or fused nucleic acid molecule of claim 47, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

49. The chimeric or fused nucleic acid molecule of claim 47, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

50. The chimeric or fused nucleic acid molecule of claim 49, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

51. The chimeric or fused nucleic acid molecule of claim 47, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

52. A nucleic acid molecule comprising the isolated cDNA of claim 42 operably linked to a heterologous promoter that is either regulatable or constitutive.

53. The nucleic acid molecule of claim 52, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

54. An isolated cDNA molecule comprising a nucleic acid sequence coding for a G protein-coupled receptor polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21.

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55. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 54.

56. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 54 under stringent hybridization conditions.

57. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 54 under moderate hybridization conditions.

58. An isolated fragment of the genomic DNA molecule of claim 54 that is at least about 20 to 30 nucleotide bases in length.

59. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 54, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

60. The chimeric or fused nucleic acid molecule of claim 59, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

61. The chimeric or fused nucleic acid molecule of claim 59, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

62. The chimeric or fused nucleic acid molecule of claim 61, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

63. The chimeric or fused nucleic acid molecule of claim 59, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

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64. A nucleic acid molecule comprising the isolated cDNA of claim 54 operably linked to a heterologous promoter that is either regulatable or constitutive.

65. The nucleic acid molecule of claim 64, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

66. An isolated cDNA molecule comprising a nucleic acid sequence having at least about 50% sequence identity to the G protein-coupled receptor polypeptide coding region in a genomic DNA sequence consisting essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20.

67. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 66.

68. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 66 under stringent hybridization conditions.

69. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 66 under moderate hybridization conditions.

70. An isolated fragment of the genomic DNA molecule of claim 66 that is at least about 20 to 30 nucleotide bases in length.

71. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 66, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

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72. The chimeric or fused nucleic acid molecule of claim 71, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

73. The chimeric or fused nucleic acid molecule of claim 71, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

74. The chimeric or fused nucleic acid molecule of claim 73, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

75. The chimeric or fused nucleic acid molecule of claim 71, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

76. A nucleic acid molecule comprising the isolated cDNA of claim 66 operably linked to a heterologous promoter that is either regulatable or constitutive.

77. The nucleic acid molecule of claim 76, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

78. An isolated cDNA molecule comprising a nucleic acid sequence having at least about 40% sequence identity to a sequence encoding a mammalian T1R G protein-coupled receptor polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 10, 12, 14, and 17.

79. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 78.

80. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 78 under stringent hybridization conditions.

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81. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 78 under moderate hybridization conditions.

82. An isolated fragment of the genomic DNA molecule of claim 78 that is at least about 20 to 30 nucleotide bases in length.

83. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 78, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

84. The chimeric or fused nucleic acid molecule of claim 83, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

85. The chimeric or fused nucleic acid molecule of claim 83, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

86. The chimeric or fused nucleic acid molecule of claim 85, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

87. The chimeric or fused nucleic acid molecule of claim 83, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

88. A nucleic acid molecule comprising the isolated cDNA of claim 78 operably linked to a heterologous promoter that is either regulatable or constitutive.

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89. The nucleic acid molecule of claim 88, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

90. An isolated variant DNA molecule comprising a nucleotide sequence consisting essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20, containing at least one conservative substitution in a region coding for a G protein-coupled receptor active in taste signaling.

91. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 90.

92. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 90 under stringent hybridization conditions.

93. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 90 under moderate hybridization conditions.

94. An isolated fragment of the genomic DNA molecule of claim 90 that is at least about 20 to 30 nucleotide bases in length.

95. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 90, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

96. The chimeric or fused nucleic acid molecule of claim 95, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

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97. The chimeric or fused nucleic acid molecule of claim 95, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

98. The chimeric or fused nucleic acid molecule of claim 97, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

99. The chimeric or fused nucleic acid molecule of claim 95, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

100. A cDNA molecule having the same nucleic acid sequence as the coding region of the variant DNA molecule of claim 90.

101. A nucleic acid molecule comprising the cDNA of claim 100 operably linked to a heterologous promoter that is either regulatable or constitutive.

102. The nucleic acid molecule of claim 101, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

103. An isolated variant molecule comprising a nucleotide sequence encoding a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21, containing at least one conservative substitution in a coding region.

104. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 103.

105. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 103 under stringent hybridization conditions.

106. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 103 under moderate hybridization conditions.

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107. An isolated fragment of the genomic DNA molecule of claim 103 that is at least about 20 to 30 nucleotide bases in length.

108. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 103, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

109. The chimeric or fused nucleic acid molecule of claim 108, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

110. The chimeric or fused nucleic acid molecule of claim 108, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

111. The chimeric or fused nucleic acid molecule of claim 110, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

112. The chimeric or fused nucleic acid molecule of claim 108, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

113. A cDNA molecule having the same nucleic acid sequence as the coding region of the variant DNA molecule of claim 103.

114. A nucleic acid molecule comprising the cDNA molecule of claim 113 operably linked to a heterologous promoter that is either regulatable or constitutive.

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115. The nucleic acid molecule of claim 114, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

116. The isolated nucleic acid molecule of claim 1, wherein said nucleic acid encodes a G protein-coupled receptor polypeptide that is active in taste signaling in rat, mouse, or human.

117. An expression vector comprising an isolated nucleic acid molecule of claim 1, wherein said vector is selected from the group consisting of mammalian vectors, bacterial plasmids, bacterial phagemids, mammalian viruses and retroviruses, bacteriophage vectors and linear or circular DNA molecules capable of integrating into a host cell genome.

118. A host cell transfected with at least one of the expression vectors of claim 117, wherein said host cell expresses the encoded G protein-coupled receptor polypeptides on the surface of said host cell.

119. A nucleic acid array comprising at least about 20 to 30 nucleotides of at least one of the isolated nucleic acid molecules of claim 1, wherein the at least one nucleic acid molecules are linked covalently or noncovalently to a solid phase support.

120. A method of screening for compounds that activate taste signaling comprising:

(i) contacting the host cell of claim 118 with a putative taste activating compound; and

(ii) measuring activity from said G protein-coupled receptor polypeptide expressed on the cell surface.

121. The method of claim 120, wherein said G protein-coupled receptor polypeptide activity is measured by assayed by measuring changes in intracellular Ca^{2+} levels, cAMP, cGMP and IP3, or G protein binding of GTPγS.

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122. The method of claim 120, wherein said host cell is transfected with at least one additional nucleic acid construct encoding a gene involved in taste signaling.

123. The method of claim 122, wherein said at least one additional gene encodes a G protein involved in taste signal transduction.

124. The method of claim 123, wherein said G protein is a promiscuous G protein.

125. A method of screening for compounds that modulate taste signaling transduction comprising:

(i) contacting a host cell according to claim 118 with a known taste activating compound and a compound putatively involved in taste transduction modulation;

(ii) contacting a host cell according to claim 118 with a known taste activating compound alone; and

(iii) comparing the activity from said G protein-coupled receptor polypeptide expressed on the cell surface of the host cell of step (i) with the activity from said G protein-coupled receptor polypeptide expressed on the cell surface of the host cell of step (ii) to identify modulators of taste transduction.

126. The method of claim 125, wherein said modulatory compounds are selected from the group consisting of activators, inhibitors, stimulators, enhancers, agonists and antagonists.

127. The method of claim 125, wherein said G protein-coupled receptor polypeptide activity is measured by assayed by measuring changes in intracellular Ca^{2+} levels, cAMP, cGMP and IP3, or G protein binding of GTPγS.

128. The method of claim 125, wherein said host cell is transfected with at least one additional nucleic acid construct encoding a gene involved in taste signaling.

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129. The method of claim 128, wherein said at least one additional gene encodes a G protein involved in taste signal transduction.

130. The method of claim 129, wherein said G protein is a promiscuous G protein.

131. A method of detecting expression of a G protein-coupled receptor polypeptide gene in a cell comprising:

(i) contacting said cell with a nucleic acid molecule that hybridizes to the isolated nucleic acid molecule of claim 1 under stringent conditions; and

(ii) detecting hybridization in order to detect expression of said G protein-coupled receptor polypeptide gene.

132. An isolated nucleic acid molecule encoding a G protein-coupled receptor polypeptide active in taste signaling having the nucleotide sequence of SEQ ID NO: 1.

133. An isolated nucleic acid molecule encoding a G protein-coupled receptor polypeptide active in taste signaling having the nucleotide sequence of SEQ ID NO: 2.

134. An isolated nucleic acid molecule encoding a G protein-coupled receptor polypeptide active in taste signaling having the nucleotide sequence of SEQ ID NO: 9.

135. An isolated nucleic acid molecule encoding a G protein-coupled receptor polypeptide active in taste signaling having the nucleotide sequence of SEQ ID NO: 11.

136. An isolated nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 3.

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137. An isolated nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 13.

138. An isolated nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 15.

139. An isolated nucleic acid molecule having the nucleotide sequence of SEQ ID NO: 16.

140. An isolated nucleic acid molecule encoding the polypeptide having the amino acid sequence of SEQ ID NO: 4.

141. An isolated nucleic acid molecule encoding the G protein-coupled receptor polypeptide active in taste signaling having the amino acid sequence of SEQ ID NO: 10.

142. An isolated nucleic acid molecule encoding the G protein-coupled receptor polypeptide active in taste signaling having the amino acid sequence of SEQ ID NO: 12.

143. An isolated nucleic acid molecule encoding the polypeptide having the amino acid sequence of SEQ ID NO: 14.

144. An isolated nucleic acid molecule encoding the polypeptide having the amino acid sequence of SEQ ID NO: 17.

145. An isolated nucleic acid molecule encoding a G protein-coupled receptor polypeptide active in taste signaling comprising the consensus sequence of SEQ ID NO: 18, or a consensus sequence having at least 75% identity to the sequence of SEQ ID NO: 18.

146. An isolated nucleic acid encoding a G protein-coupled receptor polypeptide active in taste signaling comprising the consensus sequence of SEQ

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ID NO: 19, or a consensus sequence having at least 75% identity to the sequence of SEQ ID NO: 19.

147. A genomic DNA amplified by a PCR reaction with at least one degenerate primer having a nucleic acid sequence of SEQ ID NOs 5 or 6, or consisting essentially of a nucleic acid sequence encoding a consensus sequence of SEQ ID NO 18 or 19, wherein said amplified DNA comprises a coding sequence for a G protein-coupled receptor polypeptide active in taste signaling.

148. A method for isolating a genomic sequence comprising a coding sequence for a G protein-coupled receptor polypeptide active in taste signaling, said method comprising contacting a mammalian genome with at least one degenerate primer having a nucleic acid sequence of SEQ ID NOs 5 or 6, or consisting essentially of a nucleic acid sequence encoding a consensus sequence of SEQ ID NO 18 or 19, and amplifying said genomic sequence comprising said primer sequence in the presence of polymerase, free nucleotides and cofactors.

149. A method for screening a mammalian genome for a coding sequence for a G protein-coupled receptor active in taste signaling, comprising:

(i) contacting said mammalian genome with at least one degenerate primer having a nucleic acid sequence of SEQ ID NOs 5 or 6, or consisting essentially of a nucleic acid sequence encoding a consensus sequence of SEQ ID NO 18 or 19;

(ii) amplifying said genomic sequence comprising said at least one primer sequence in the presence of polymerase, free nucleotides and cofactors; and

(iii) detecting the presence of an amplified sequence comprising a G protein-coupled receptor polypeptide gene.

150. Plasmid SAV115 comprising a mouse T1R3 gene.

151. Plasmid SAV118 comprising a rat T1R3 gene.

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152. An isolated polypeptide selected from the group consisting of:

(i) a G protein-coupled receptor polypeptide active in taste signaling encoded by a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs 9 and 11, and genomic sequences consisting essentially of SEQ ID NOs 1, and 2;

(ii) a G protein-coupled receptor polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20, and a genomic sequence consisting essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20;

(iii) a G protein-coupled receptor polypeptide active in taste signaling comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 10 and 12;

(iv) a G protein-coupled receptor polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21;

(v) a G protein-coupled receptor polypeptide active in taste signaling encoded by a nucleic acid molecule comprising a nucleic acid sequence having at least about 50% identify to a nucleic acid sequence selected from the group consisting of SEQ ID NOs 9 and 11, and genomic sequences consisting essentially of SEQ ID NOs 1, and 2;

(vi) a G protein-coupled receptor polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence having at least about 50% identify to a nucleic acid sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20, and a genomic sequence consisting essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20;

(vii) a G protein-coupled receptor polypeptide active in taste signaling comprising an amino acid sequence that is at least about 40% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs 10 and 12;

(viii) a G protein-coupled receptor polypeptide comprising an amino acid sequence that is at least about 40% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21;

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(ix) a variant of a G protein-coupled receptor polypeptide active in taste signaling encoded by a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs 9 and 11, and genomic sequences consisting essentially of SEQ ID NOs 1, and 2, wherein said variant protein contains at least one conservative substitution relative to the G protein-coupled receptor encoded by said nucleotide sequence;

(x) a variant a G protein-coupled receptor polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20, and a genomic sequence consisting essentially of a nucleic acid sequence selected from the group consisting of SEQ ID NOs 15 and 20, wherein said variant protein contains at least one conservative substitution relative to the G protein-coupled receptor encoded by said nucleotide sequence;

(xi) a variant of a G protein-coupled receptor polypeptide active in taste signaling comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 10 and 12, containing at least one conservative substitution; and

(xii) a variant of a G protein-coupled receptor polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 4, 14, 17, and 21, containing at least one conservative substitution.

153. A fragment of the polypeptide of claim 152, wherein said fragment comprises at least about 5 to 7 amino acids.

154. The fragment of claim 153, wherein said fragment contains an extracellular domain of a T1R mammalian G protein-coupled receptor polypeptide.

155. The fragment of claim 154, wherein said extracellular domain interacts with a compound involved in taste activation or modulation.

156. The fragment of claim 154, wherein said extracellular domain interacts with a protein involved in taste signal transduction.

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157. The fragment of claim 156, wherein said protein involved in taste signal transduction is a G protein subunit.

158. The fragment of claim 157, wherein said G protein subunit is a promiscuous G protein.

159. A chimeric or fusion polypeptide comprising at least part of the amino acid sequence of a polypeptide of claim 152, and at least part of a heterologous amino acid sequence.

160. The chimeric or fusion polypeptide of claim 159, wherein said heterologous sequence is a sequence from a different G protein-coupled receptor.

161. The chimeric or fusion polypeptide of claim 159, wherein said heterologous sequence is a sequence from green fluorescent protein.

162. A method of screening one or more compounds for the presence of a compound that activates or modulates taste signaling, comprising contacting said one or more compounds with one or more fragments of one or more polypeptides according to claim 152, wherein the one or more fragments are at least about a 5 to 7 amino acids in length.

163. A method for screening one or more proteins for the presence of a protein that interacts with a G protein-coupled receptor active in taste signaling, comprising contacting said one or more proteins with one or more fragments of one or more polypeptides according to claim 152, wherein the one or more fragments are at least about a 5 to 7 amino acids in length.

164. A polypeptide array comprising at least about a 5 to 7 amino acid segment of one or more polypeptides according to claim 152, wherein said one or more polypeptide segments are linked covalently or noncovalently to a solid phase support.

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165. An isolated antibody or antibody fragment that binds with specificity to a polypeptide of claim 152.

166. An isolated polypeptide having the amino acid sequence of SEQ ID NO: 4.

167. An isolated polypeptide having the amino acid sequence of SEQ ID NO: 10.

168. An isolated polypeptide having the amino acid sequence of SEQ ID NO: 12.

169. An isolated polypeptide having the amino acid sequence of SEQ ID NO: 14.

170. An isolated polypeptide having the amino acid sequence of SEQ ID NO: 17.

171. A method for representing the perception of one or more tastes in one or more mammals, comprising the steps of:

(i) providing values X_1 to X_n representative of the quantitative stimulation of each of n taste receptors of said mammals; and

(ii) generating from said values a quantitative representation of taste perception, wherein at least one of said taste receptors is a taste receptor polypeptide having a sequence that is at least about 40% identical to a sequence selected from the group consisting of SEQ ID NOs 4, 10, 12, 14, and 17.

172. The method of claim 171, wherein said representation constitutes a point or a volume in n-dimensional space.

173. The method of claim 171, wherein said representation constitutes a graph or a spectrum.

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174. The method of claim 171, wherein said representation constitutes a matrix of quantitative representations.

175. The method of claim 171, wherein said providing step comprises contacting a plurality of recombinantly produced taste receptors with a test composition and quantitatively measuring the interaction of said composition with said receptors.

176. A method for predicting the taste perception in a mammal generated by one or more molecules or combinations of molecules comprising the steps of:

(i) providing values X_1 to X_n representative of the quantitative stimulation of each of n taste receptors of said mammal, for one or more molecules or combinations of molecules yielding known taste perception in a mammal,

(ii) generating from said values a quantitative representation of taste perception in a mammal for the one or more molecules or combinations of molecules yielding known taste perception in a mammal;

(iii) providing values X_1 to X_n representative of the quantitative stimulation of each of n taste receptors of said mammal, for one or more molecules or combinations of molecules yielding unknown taste perception in a mammal,

(iv) generating from said values a quantitative representation of taste perception in a mammal for the one or more molecules or combinations of molecules yielding unknown taste perception in a mammal; and

(v) predicting the taste perception in a mammal generated by one or more molecules or combinations of molecules yielding unknown taste perception in a mammal by comparing the quantitative representation of taste perception in a mammal generated by one or more molecules or combinations of molecules yielding unknown taste perception in a mammal to the quantitative representation of taste perception in a mammal for the one or more molecules or combinations of molecules yielding known taste perception in a mammal,

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wherein at least one of said taste receptors is a taste receptor polypeptide having a sequence that is at least about 40% identical to a sequence selected from the group consisting of SEQ ID NOs 4, 10, 12, 14, and 17.

177. A genomic DNA molecule consisting essentially of a nucleic acid sequence coding for a mammalian G protein-coupled receptor polypeptide active in taste signaling comprising a consensus sequence selected from the group consisting of SEQ ID NOs 18 and 19, and sequences having at least about 75% identity to SEQ ID NOs 18 or 19.

178. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 177.

179. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 177 under stringent hybridization conditions.

180. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 177 under moderate hybridization conditions.

181. An isolated fragment of the genomic DNA molecule of claim 177 that is at least about 20 to 30 nucleotide bases in length.

182. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 177, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

183. The chimeric or fused nucleic acid molecule of claim 182, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

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184. The chimeric or fused nucleic acid molecule of claim 182, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

185. The chimeric or fused nucleic acid molecule of claim 184, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

186. The chimeric or fused nucleic acid molecule of claim 182, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

187. A cDNA sequence coding for a mammalian G protein-coupled receptor polypeptide active in taste signaling comprising a consensus sequence selected from the group consisting of SEQ ID NOs 18 and 19, and sequences having at least about 75% identity to SEQ ID NOs 18 or 19.

188. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 187.

189. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 187 under stringent hybridization conditions.

190. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 187 under moderate hybridization conditions.

191. An isolated fragment of the genomic DNA molecule of claim 187 that is at least about 20 to 30 nucleotide bases in length.

192. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 187, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

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193. The chimeric or fused nucleic acid molecule of claim 192, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

194. The chimeric or fused nucleic acid molecule of claim 192, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

195. The chimeric or fused nucleic acid molecule of claim 194, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

196. The chimeric or fused nucleic acid molecule of claim 192, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

197. A nucleic acid molecule comprising the isolated cDNA of claim 187 operably linked to a heterologous promoter that is either regulatable or constitutive.

198. The nucleic acid molecule of claim 197, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

199. A cDNA molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20.

200. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 199.

201. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 199 under stringent hybridization conditions.

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202. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 199 under moderate hybridization conditions.

203. An isolated fragment of the genomic DNA molecule of claim 199 that is at least about 20 to 30 nucleotide bases in length.

204. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 199, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

205. The chimeric or fused nucleic acid molecule of claim 204, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

206. The chimeric or fused nucleic acid molecule of claim 204, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

207. The chimeric or fused nucleic acid molecule of claim 206, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

208. The chimeric or fused nucleic acid molecule of claim 204, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

209. A nucleic acid molecule comprising the isolated cDNA of claim 199 operably linked to a heterologous promoter that is either regulatable or constitutive.

210. The nucleic acid molecule of claim 209, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

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211. A cDNA molecule comprising a nucleic acid sequence having at least about 50% identity to a sequence selected from the group consisting of SEQ ID NOs 3, 13, 16, and 20.

212. An isolated RNA molecule transcribed from the isolated DNA molecule of claim 211.

213. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 211 under stringent hybridization conditions.

214. An isolated nucleic acid molecule that hybridizes to the DNA molecule of claim 211 under moderate hybridization conditions.

215. An isolated fragment of the genomic DNA molecule of claim 211 that is at least about 20 to 30 nucleotide bases in length.

216. A chimeric or fused nucleic acid molecule, wherein said chimeric or fused nucleic acid molecule comprises at least part of the coding sequence contained in the DNA molecule of claim 211, and at least part of a heterologous coding sequence, wherein transcription of said chimeric or fused nucleic acid molecule results in a single chimeric nucleic acid transcript.

217. The chimeric or fused nucleic acid molecule of claim 216, wherein said heterologous coding sequence is from a sequence encoding a different G protein-coupled receptor.

218. The chimeric or fused nucleic acid molecule of claim 216, wherein said heterologous coding sequence is a sequence that facilitates expression of said mammalian G protein-coupled receptor polypeptide on the surface of a cell.

219. The chimeric or fused nucleic acid molecule of claim 218, wherein said heterologous coding sequence is from a mammalian rhodopsin gene.

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220. The chimeric or fused nucleic acid molecule of claim 216, wherein said heterologous coding sequence is from a gene encoding green fluorescent protein or other detectable marker gene.

221. A nucleic acid molecule comprising the isolated cDNA of claim 211 operably linked to a heterologous promoter that is either regulatable or constitutive.

222. The nucleic acid molecule of claim 221, wherein said regulatable promoter is inducible under specific environmental or developmental conditions.

223. The fragment of claim 153, wherein said fragment includes at least an N-terminal fragment of a G protein-coupled receptor.

224. The fragment of claim 223, wherein said N-terminal fragment is involved in ligand binding.

225. The polypeptide fragment of claim 224, wherein said fragment is at least about 100 amino acids in length.

226. The polypeptide fragment of claim 224, wherein said fragment is at least about 600 amino acids in length.

227. A biochemical assay for identifying taste stimulus ligands having binding specificity for a G protein-coupled receptor active in taste signaling, comprising:

(i) contacting one or more fragments according to claim 224 with one or more putative taste stimulus ligands or a composition comprising one or more putative taste stimulus ligands; and

(ii) detecting binding of a taste stimulus ligand having binding specificity for said G protein-coupled receptor active in taste signaling.

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228. The assay of claim 227, wherein binding is detected by displacement of a radiolabeled known binding ligand.

229. The assay of claim 228, wherein said known binding ligand is an antibody or antibody fragment having binding specificity to said G protein-coupled receptor.

230. An isolated nucleic acid molecule having the nucleic acid sequence of SEQ ID NO 20.

231. A chimeric or fusion polypeptide comprising at least an extracellular domain of at least one polypeptide according to claim 152, and at least part of a heterologous amino acid sequence.

232. The chimeric or fusion polypeptide of claim 231, wherein said heterologous amino acid sequence is a sequence from a different G protein-coupled receptor.

233. The chimeric or fusion polypeptide of claim 232, wherein said different G protein-coupled receptor is a T1R mammalian G protein-coupled receptor, and said heterologous amino acid sequence includes at least an extracellular domain of said T1R mammalian G protein-coupled receptor.

234. A biochemical assay for identifying taste stimulus ligands having binding specificity for a G protein-coupled receptor active in taste signaling, comprising:

(i) contacting one or more fragments according to claim 224 with a preparation of G proteins and GTPγS, and one or more putative taste stimulus ligands or a composition comprising one or more putative taste stimulus ligands; and

(ii) detecting binding of a taste stimulus ligand having binding specificity for said G protein-coupled receptor active in taste signaling by measuring the binding of GTPγS to the G protein.

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Figure 1. Human T1R2/T1R3 functions as a sweet taste receptor

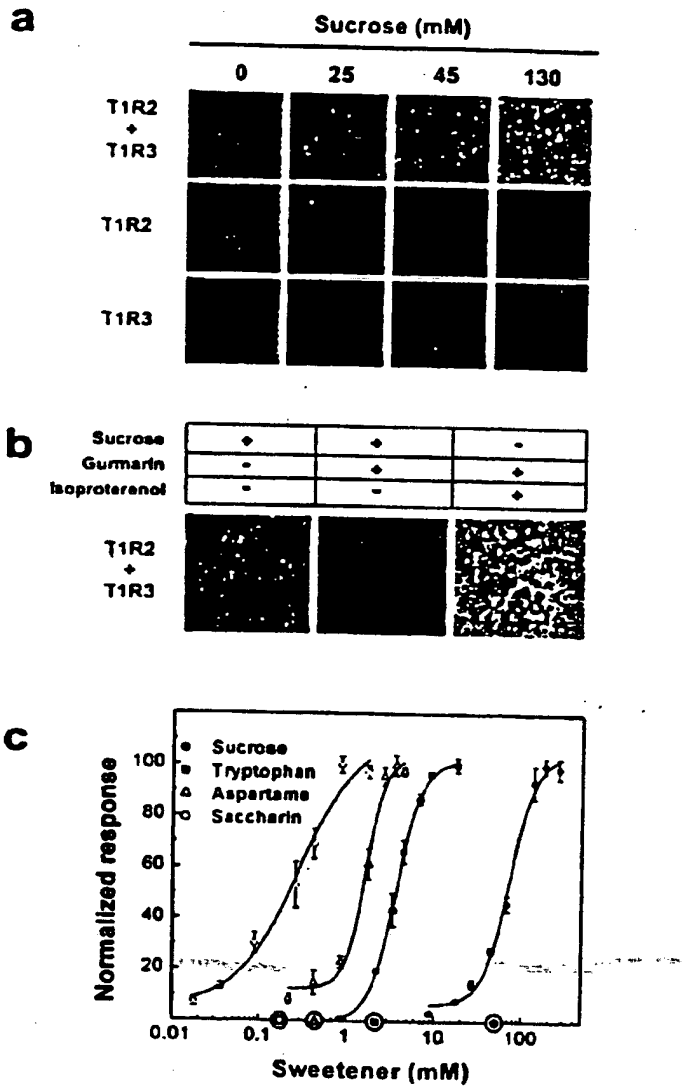

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Figure 2 T1R2 may control T1R2/T1R3 ligand specificity

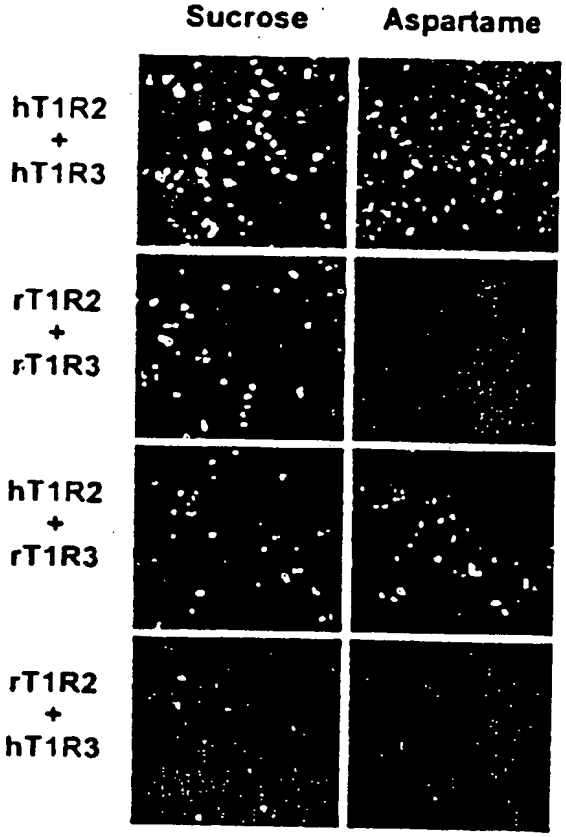

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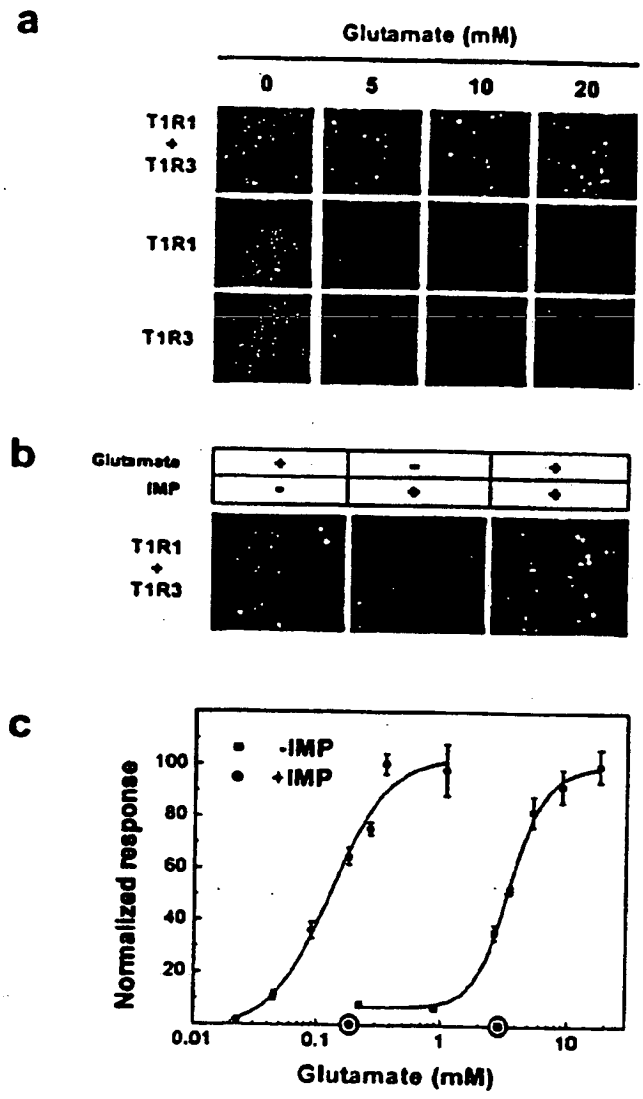
Figure 3. Human T1R1/T1R3 functions as an umami taste receptor



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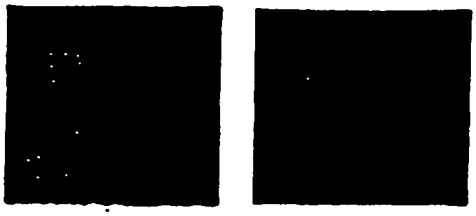

H2-IT-Myc H2-PDZIP-IT-Myc

B.

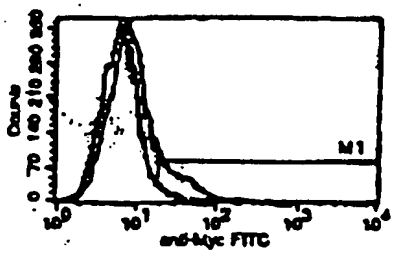

Figure 4 PDZIP facilitate the surface expression of human T1R2.

A. Immunofluorescence staining of Myc-tagged hT1R2 indicates that PDZIP significantly increases the amount of human T1R2 protein on the plasma membrane (Staszewski, May 15th, 2001, Notebook No. 2, page 76-77).

B. FACS analysis data demonstrating the same result (Staszewski, June 4th, 2001, Notebook No. 2, page 79). Myc-tagged human T1R2: Green line. Myc-tagged humanT1R2 with PDZIP: black line.

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Figure 5

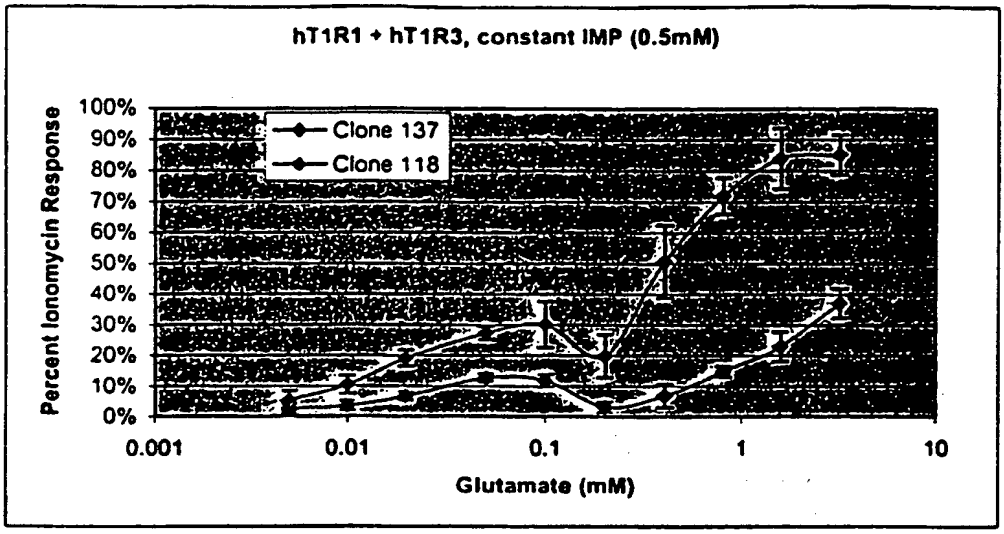
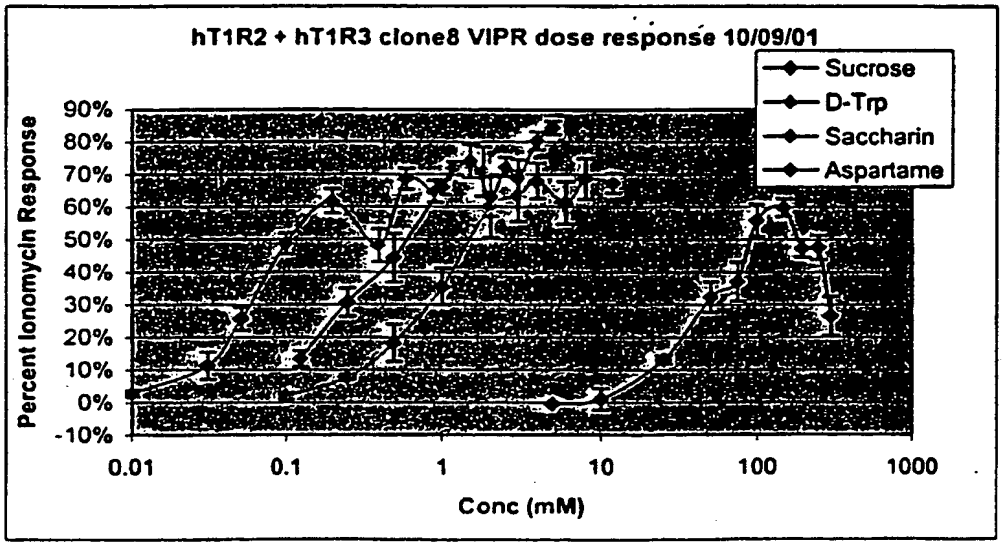


Figure 6



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